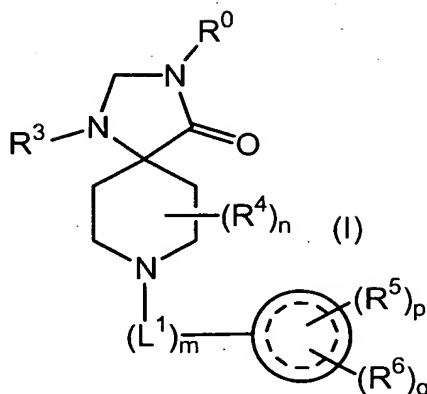


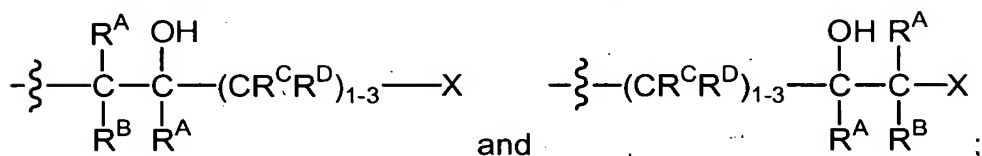
What is claimed is:

1. A compound of the formula (I)



- 5 wherein

$R^0$  is selected from the group consisting of



each  $R^A$  and  $R^B$  is independently selected from the group consisting of hydrogen and  $C_{1-4}$ alkyl;

- 10 each  $R^C$  and  $R^D$  is independently selected from the group consisting of hydrogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, nitro, cyano,  $N(R^E)_2$ , aryl,  $arC_{1-4}$ alkyl, heteroaryl or heterocycloalkyl; wherein the aryl,  $arC_{1-4}$ alkyl, heteroaryl or heterocycloalkyl substituent is optionally substituted with one or more substituents independently selected from hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, nitro, cyano or  $N(R^E)_2$ ;

15 each  $R^E$  is independently selected from the group consisting of hydrogen and  $C_{1-4}$ alkyl;

- 20 X is selected from the group consisting of  $-NR^1R^2$ ,  $-C(O)-NR^1R^2$ ,  $-NR^1-C(O)-R^2$ ,  $-OR^1$ ,  $-SR^1$ ,  $-SOR^1$ ,  $-SO_2R^1$ ,  $-S-(C_{2-4}alkyl)-NR^1R^2$ ,  $-S-(C_{2-4}alkyl)-C(O)O-C(CH_3)_3$ ,  $-SO-(C_{1-4}alkyl)-NR^1R^2$  and  $-SO_2-(C_{1-4}alkyl)-NR^1R^2$ ; wherein the alkyl portion of the  $-S-(C_{2-4}alkyl)-NR^1R^2$ ,  $-SO-(C_{1-4}alkyl)-NR^1R^2$  or  $-SO_2-(C_{1-4}alkyl)-NR^1R^2$  group is optionally substituted with one or more substituents independently selected from carboxy, hydroxy, hydroxy $C_{1-4}$ alkyl,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxycarbonyl or  $-CONR^1R^2$ ;

each  $R^1$  and  $R^2$  is independently selected from the group consisting of hydrogen,  $C_{1-8}$ alkyl,  $C_{1-8}$ alkoxy,  $C_{1-8}$ alkoxycarbonyl, cycloalkyl, cycloalkyl- $C_{1-4}$ alkyl, partially unsaturated carbocyl, partially unsaturated carbocycl- $C_{1-4}$ alkyl, aryl, ar $C_{1-4}$ alkyl, ar $C_{1-4}$ alkoxy, heteroaryl, heteroaryl- $C_{1-4}$ alkyl, heterocycloalkyl, heterocycloalkyl- $C_{1-4}$ alkyl, -C(O)- $C_{1-6}$ alkyl, -C(O)-aryl, -C(O)-ar $C_{1-4}$ alkyl, -C(O)-heteroaryl, -C(O)-heterocycloalkyl, -C(O)O-cycloalkyl and -C(O)O-aryl, -C(O)O-ar $C_{1-4}$ alkyl, -C(O)O-(partially unsaturated carbocycl), -C(O)O-heteroaryl, -C(O)O-heterocycloalkyl; wherein the  $C_{1-8}$ alkyl, cycloalkyl, partially unsaturated carbocycl, aryl, ar $C_{1-8}$ alkyl, heteroaryl or heterocycloalkyl group, whether alone or part of a substituent group, is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, -C(O)- $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxycarbonyl,  $N(R^E)_2$ ,  $N(R^E)_2$ - $C_{1-4}$ alkyl,  $N(R^E)$ -C(O)C(CH<sub>3</sub>)<sub>3</sub>, - $C_{1-4}$ alkyl- $N(R^E)$ -C(O)O- $C_{1-4}$ alkyl and + $N(R^E)$ -C(O)O- $C_{1-4}$ alkyl, aryl, aryloxy, cycloalkyl, heteroaryl, aryl substituted heteroarylamino-sulfonyl or  $C_{1-6}$ alkylthio;

alternatively when  $R^1$  and  $R^2$  are both bound to the same nitrogen atom,  $R^1$  and  $R^2$  are taken together with the nitrogen atom to which they are bound to form a heteroaryl or heterocycloalkyl group; wherein the heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl, hydroxy substituted  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $C_{1-4}$ alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, nitro, cyano,  $N(R^E)_2$ , aryl, ar $C_{1-4}$ alkyl, heteroaryl, heterocycloalkyl, di( $C_{1-6}$ )alkylamino-carbonyl,  $C_{1-4}$ alkoxycarbonyl- $N(R^E)$ - or arylamino- $C_{1-4}$ alkyl; wherein the aryl, ar $C_{1-4}$ alkyl, heteroaryl or heterocycloalkyl substituent is optionally further substituted with one or more substituents independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano,  $N(R^E)_2$ , phenyl or substituted phenyl; wherein the substituents on the phenyl are one or more independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or  $N(R^E)_2$ ;

$R^3$  is selected from the group consisting of aryl, ar $C_{1-6}$ alkyl and heteroaryl; wherein the aryl, ar $C_{1-6}$ alkyl or heteroaryl group is optionally

substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or N(R<sup>E</sup>)<sub>2</sub>;

n is an integer from 0 to 2;

- 5 R<sup>4</sup> is selected from the group consisting of hydroxy, C<sub>1-4</sub>alkyl and hydroxy substituted C<sub>1-4</sub>alkyl;

m is an integer from 0 to 1;

- L<sup>1</sup> is selected from the group consisting of C<sub>1-6</sub>alkyl and C<sub>3-6</sub>alkenyl; wherein the double bond of the C<sub>3-6</sub>alkenyl group is at least one carbon atom removed from the attachment point to the N atom; and wherein the C<sub>1-6</sub>alkyl or C<sub>3-6</sub>alkenyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C<sub>1-6</sub>alkyl, fluorinated C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkoxy;



- 15 is selected from the group consisting of cycloalkyl, partially unsaturated carbocyclyl, aryl, heteroaryl and heterocycloalkyl;

p is an integer from 0 to 5;

- R<sup>5</sup> is selected from the group consisting of hydroxy, carboxy, halogen, C<sub>1-6</sub>alkyl, hydroxy substituted C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, nitro, cyano, NR<sup>1</sup>R<sup>2</sup>, trifluoromethyl, trifluoromethoxy, C<sub>1-4</sub>alkoxycarbonyl, -SO-NR<sup>1</sup>R<sup>2</sup>, -SO<sub>2</sub>-NR<sup>1</sup>R<sup>2</sup> and -C(O)-NR<sup>1</sup>R<sup>2</sup>;

q is an integer from 0 to 1;

R<sup>6</sup> is selected from the group consisting of -(L<sup>2</sup>)<sub>0-1</sub>-R<sup>7</sup>;

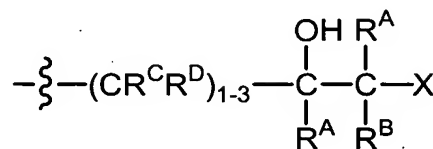
- L<sup>2</sup> is selected from the group consisting of -C<sub>1-6</sub>alkyl-, -C<sub>2-4</sub>alkenyl-, -C<sub>2-6</sub>alkynyl-, -O-, -S-, -NH-, -N(C<sub>1-4</sub>alkyl)-, -C<sub>1-6</sub>alkyl-O-, -C<sub>1-6</sub>alkyl-S-, -O-C<sub>1-6</sub>alkyl-, -S-C<sub>1-6</sub>alkyl-, -O-C<sub>2-6</sub>alkyl-O-, -S-C<sub>2-6</sub>alkyl-S-, -SO<sub>2</sub>-, -SO<sub>2</sub>NH-, -SO<sub>2</sub>N(C<sub>1-4</sub>alkyl)-, -NH-SO<sub>2</sub>-, -N(C<sub>1-4</sub>alkyl)-SO<sub>2</sub>-, -C(O)-O- and -O-C(O)-;

- R<sup>7</sup> is selected from the group consisting of aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl and heterocycloalkyl; wherein the aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, halogen, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, nitro, cyano,

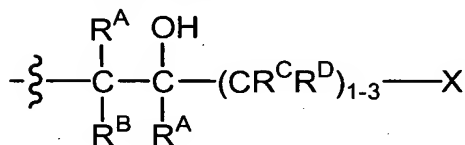
$N(R^E)_2$ , trifluoromethyl, trifluoromethoxy,  $C_{1-4}$ alkoxycarbonyl,  $-SO_2-N(R^E)_2$  and  $-C(O)-N(R^E)_2$ ;

or a pharmaceutically acceptable salt thereof.

- 5 2. A compound as in Claim 1 wherein



$R^0$  is selected from the group consisting of



and

- each  $R^C$  and  $R^D$  is independently selected from hydrogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, hydroxy, carboxy or aryl; wherein the aryl is optionally substituted with  
 10 one to two substituents independently selected from hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, nitro, cyano or  $N(R^E)_2$ ;

- X is selected from the group consisting of  $-NR^1R^2$ ,  $-C(O)-NR^1R^2$ ,  $-NR^1-C(O)-R^2$ ,  $-OR^1$ ,  $-SR^1$ ,  $-SO-R^1$ ,  $-SO_2-R^1$ ,  $-S-(C_{2-4}\text{alkyl})-NR^1R^2$ ,  $-S-(C_{2-4}\text{alkyl})-NR^1-C(O)OC(CH_3)_3$ ,  $-SO-(C_{1-4}\text{alkyl})-NR^1R^2$  and  $-SO_2-(C_{1-4}\text{alkyl})-NR^1R^2$ ; wherein the  
 15 alkyl portion of the  $-S-(C_{2-4}\text{alkyl})-NR^1R^2$ ,  $-SO-(C_{1-4}\text{alkyl})-NR^1R^2$  or  $-SO_2-(C_{1-4}\text{alkyl})-NR^1R^2$  group is optionally substituted with one to two substituents independently selected from  $C_{1-4}$ alkyl, hydroxy $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxycarbonyl or carboxy;

- $R^1$  is selected from the group consisting of hydrogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $C_{1-4}$ alkoxycarbonyl, aryl,  $arC_{1-4}$ alkyl,  $arC_{1-4}$ alkyloxy, heteroaryl, heteroaryl-alkyl, heterocycloalkyl, heterocycloalkyl-alkyl, cycloalkyl-alkyl,  $C(O)-C_{1-4}$ alkyl and  $-C(O)-$ heteroaryl;  
 20

- wherein the  $C_{1-4}$ alkyl, aryl,  $arC_{1-4}$ alkyl, heteroaryl, heterocycloalkyl or cycloalkyl group, whether alone or part of a substituent group, is optionally  
 25 substituted with one to three substituents independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $C_{1-4}$ alkoxycarbonyl,  $N(R^E)_2$ ,  $N(R^E)_2-C_{1-4}$ alkyl,  $N(R^E)-C(O)OC(CH_3)_3$ , nitro, trifluoromethyl, trifluoromethoxy, phenyl,

phenoxy, heteroaryl, cycloalkyl, 1-phenyl-pyrazol-2-yl-aminosulfonyl or C<sub>1-4</sub>alkylthio;

R<sup>2</sup> is selected from the group consisting of hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, cycloalkyl, cycloalkyl-C<sub>1-4</sub>alkyl, aryl, arC<sub>1-4</sub>alkyl, arC<sub>1-4</sub>alkyloxy, partially  
 5 unsaturated carbocyclyl, partially unsaturated carbocyclyl-C<sub>1-4</sub>alkyl, heteroaryl, heteroaryl-C<sub>1-4</sub>alkyl, heterocycloalkyl, heterocycloalkyl-C<sub>1-4</sub>alkyl, -C(O)-C<sub>1-4</sub>alkyl, -C(O)-aryl, -C(O)-arC<sub>1-4</sub>alkyl, -C(O)-heteroaryl, -C(O)-heterocycloalkyl, -C(O)O-cycloalkyl and -C(OO)-C<sub>1-4</sub>alkyl;

wherein the C<sub>1-4</sub>alkyl, aryl, arC<sub>1-4</sub>alkyl, partially unsaturated carbocyclyl,  
 10 heteroaryl, heterocycloalkyl or cycloalkyl group, whether alone or part of a substituent group, is optionally substituted with one to three substituents independently selected from halogen, hydroxy, carboxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxycarbonyl, N(R<sup>E</sup>)<sub>2</sub>, N(R<sup>E</sup>)<sub>2</sub>-C<sub>1-4</sub>alkyl, (CH<sub>3</sub>)<sub>3</sub>COC(O)-N(R<sup>E</sup>)-C<sub>1-4</sub>alkyl, nitro, cyano, trifluoromethyl, trifluoromethoxy, phenyl, phenoxy, heteroaryl,  
 15 cycloalkyl, 1-phenyl substituted heteroaryl-aminosulfonyl, -C(O)-C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkylthio;

alternatively when R<sup>1</sup> and R<sup>2</sup> are both bound to the same nitrogen atom, R<sup>1</sup> and R<sup>2</sup> are taken together with the nitrogen atom to which they are bound to  
 20 form a heteroaryl or heterocycloalkyl group;

wherein the heteroaryl or heterocycloalkyl is optionally substituted with one to three substituents independently selected from halogen, hydroxy, carboxy, C<sub>1-4</sub>alkyl, hydroxy substituted C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, nitro, cyano, N(R<sup>E</sup>)<sub>2</sub>, phenyl, arC<sub>1-4</sub>alkyl,  
 25 heterocycloalkyl, di(C<sub>1-4</sub>alkyl)amino-carbonyl, C<sub>1-4</sub>alkoxycarbonylamino or phenylamino-C<sub>1-4</sub>alkyl;

wherein the phenyl or arC<sub>1-4</sub>alkyl substituent on the heteroaryl or heterocycloalkyl group is optionally substituted with one or two substituents independently selected from halogen, hydroxy, carboxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano, N(R<sup>E</sup>)<sub>2</sub> or substituted phenyl;  
 30 wherein the substituents on the phenyl are one to three independently selected from halogen;

$R^3$  is selected from the group consisting of aryl and arC<sub>1-4</sub>alkyl; wherein the aryl or arC<sub>1-4</sub>alkyl group is optionally substituted with one to three substituents independently selected from halogen, hydroxy, carboxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or N(R<sup>E</sup>)<sub>2</sub>;

5             $n$  is an integer from 0 to 1;

$L^1$  is C<sub>1-4</sub>alkyl; wherein the C<sub>1-4</sub>alkyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C<sub>1-4</sub>alkyl, fluorinated C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkoxy;

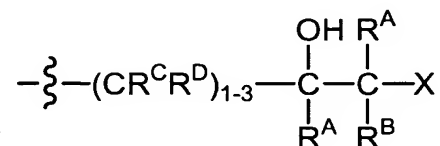
$R^5$  is selected from the group consisting of hydroxy, carboxy, halogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, nitro, cyano, N(R<sup>E</sup>)<sub>2</sub>, trifluoromethyl, trifluoromethoxy, C<sub>1-4</sub>alkoxycarbonyl, -SO- N(R<sup>E</sup>)<sub>2</sub>, -SO<sub>2</sub>- N(R<sup>E</sup>)<sub>2</sub> and -C(O)- N(R<sup>E</sup>)<sub>2</sub>;

$L^2$  is selected from the group consisting of -C<sub>1-4</sub>alkyl-, -O-, -S-, -N(R<sup>E</sup>)-, -C(O)O- and -O-C(O)-;

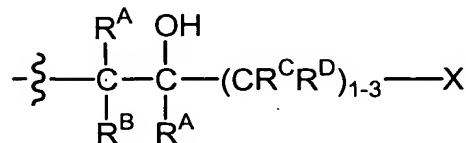
$R^7$  is selected from the group consisting of cycloalkyl, aryl, heteroaryl and heterocycloalkyl; wherein the aryl, heteroaryl or heterocycloalkyl group is optionally substituted with one to two substituents independently selected from hydroxy, carboxy, halogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, nitro, cyano, N(R<sup>E</sup>)<sub>2</sub>, trifluoromethyl, trifluoromethoxy or C<sub>1-4</sub>alkoxycarbonyl; or a pharmaceutically acceptable salt thereof.

20

3. A compound as in Claim 2 wherein



$R^0$  is selected from the group consisting of



and

each  $R^A$ ,  $R^B$ ,  $R^C$  and  $R^D$  is hydrogen;

25             $X$  is selected from the group consisting of -NR<sup>1</sup>R<sup>2</sup>, -OR<sup>1</sup>, -SR<sup>1</sup>, -S-(C<sub>2-4</sub>alkyl)-NR<sup>1</sup>R<sup>2</sup> and -S-(C<sub>2-4</sub>alkyl)-NR<sup>1</sup>-C(O)O-C(CH<sub>3</sub>)<sub>3</sub>; wherein the alkyl portion of the -S-(C<sub>2-4</sub>alkyl)-NR<sup>1</sup>R<sup>2</sup> or -S-(C<sub>1-4</sub>alkyl)-NR<sup>1</sup>-C(O)O-C(CH<sub>3</sub>)<sub>3</sub> group is optionally substituted with a carboxy or C<sub>1-4</sub>alkoxycarbonyl group;

$R^1$  is selected from the group consisting of hydrogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxycarbonyl,  $arC_{1-4}$ alkyl and  $C(O)-C_{1-4}$ alkyl;

wherein the  $C_{1-4}$ alkyl or aryl group, whether alone or part of a substituent group, is optionally substituted with one to two substituents independently

5 selected from carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $C_{1-4}$ alkoxycarbonyl,  $N(R^E)_2$  or  $N(R^E)-C(O)OC(CH_3)_3$ ;

$R^2$  is selected from the group consisting of hydrogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, cycloalkyl, aryl,  $arC_{1-4}$ alkyl,  $arC_{1-4}$ alkyloxy, partially unsaturated carbocyclyl, partially unsaturated carbocyclyl- $C_{1-4}$ alkyl, heteroaryl, heteroaryl-  
10  $C_{1-4}$ alkyl, heterocycloalkyl, heterocycloalkyl- $C_{1-4}$ alkyl, cycloalkyl- $C_{1-4}$ alkyl,  $-C(O)arC_{1-4}$ alkyl,  $-C(O)-heteroaryl$ ,  $-C(OO)-cycloalkyl$  and  $-C(O)O-C_{1-4}$ alkyl;

wherein the  $C_{1-4}$ alkyl, aryl,  $arC_{1-4}$ alkyl, partially unsaturated carbocyclyl, heteroaryl, heterocycloalkyl or cycloalkyl group, whether alone or part of a substituent group, is optionally substituted with one to three substituents  
15 independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $C_{1-4}$ alkoxycarbonyl,  $N(R^E)_2$ ,  $N(R^E)_2-C_{1-4}$ alkyl,  $(CH_3)_3CO-C(O)-N(R^E)-C_{1-4}$ alkyl, nitro, trifluoromethyl, trifluoromethoxy, phenyl, phenoxy, heteroaryl, cycloalkyl, 1-phenyl-pyrazol-2-yl-aminosulfonyl or  $C_{1-4}$ alkylthio;

20 alternatively when  $R^1$  and  $R^2$  are both bound to the same nitrogen atom,  $R^1$  and  $R^2$  are taken together with the nitrogen atom to which they are bound to form a group selected from heterocycloalkyl and heteroaryl;

wherein the heteroaryl or heterocycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, carboxy,  $C_{1-4}$ alkyl, hydroxy substituted  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, phenyl,  $arC_{1-4}$ alkyl, heterocycloalkyl,  $C_{1-4}$ alkoxycarbonyl, amino,  $C_{1-4}$ alkylamino,  $di(C_{1-4}alkyl)amino$ ,  $di(C_{1-4}alkyl)amino-carbonyl$ , t-butoxycarbonylamino or phenylamino- $C_{1-4}$ alkyl;

wherein the phenyl or  $arC_{1-4}$ alkyl substituent is optionally substituted with one or two substituents independently selected from chloro, trifluoromethyl or chlorophenyl;  
30

$R^3$  is aryl; wherein the aryl group is optionally substituted with one or more substituents independently selected from halogen;

n is 0;

$L^1$  is  $C_{1-4}$ alkyl;

$R^5$  is selected from the group consisting of halogen,  $C_{1-4}$ alkyl and trifluoromethyl;

$R^6$  is  $-(L^2)_0-R^7$ ;

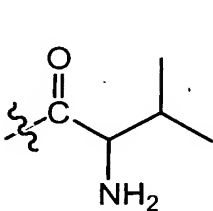
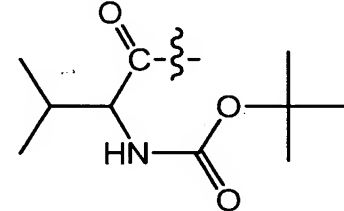
- 5  $R^7$  is selected from the group consisting of aryl and heteroaryl; or a pharmaceutically acceptable salt thereof.

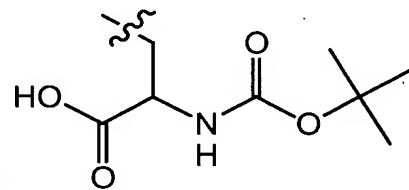
4. A compound as in Claim 3 wherein

- 10  $R^0$  is selected from the group consisting of  $-\text{CH}_2\text{-CH(OH)-CH}_2\text{-X}$  and  $-\text{CH}_2\text{-CH}_2\text{-CH(OH)-CH}_2\text{-X}$ ;

X is selected from the group consisting of  $-\text{NR}^1\text{R}^2$ ,  $-\text{OR}^1$ ,  $-\text{SR}^1$ ,  $-\text{S-CH}_2\text{CH(CO}_2\text{H)-NH-C(O)-CH}_3$  and  $-\text{S-CH}_2\text{CH(CO}_2\text{H)-NH-C(O)OC(CH}_3\text{)}_3$ ;

$R^1$  is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, t-butyl, amino-n-propyl, dimethylaminoethyl, benzyl,

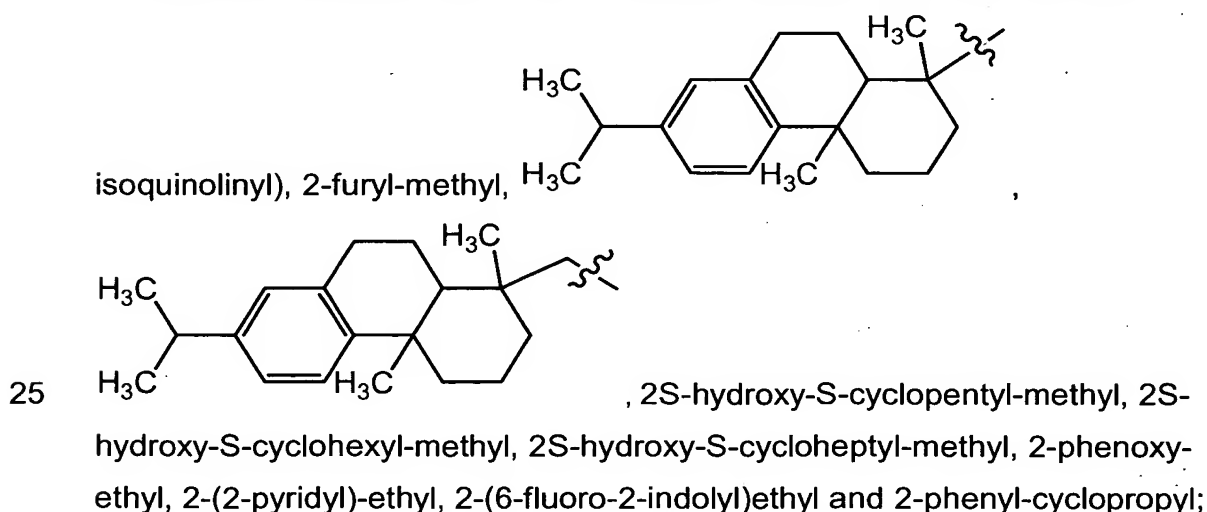
- 15 phenylethyl, 4-methyl-benzyl, , , 2-(3,4-dimethoxy-phenyl)ethyl, 3-methyl-phenyl, ethoxy-carbonyl-methyl, 2-amino-2-

methoxycarbonyl-ethyl, t-butoxycarbonyl and  ;

- 20  $R^2$  is selected from the group consisting of hydrogen, methyl, methoxy, ethyl, carboxy-methyl, ethoxycarbonylmethyl, 2,2,2-trifluoroethyl, ethoxy, dimethylaminoethyl, t-butoxycarbonylamino-ethyl, n-butyl, t-butyl, n-propyl, 3-hydroxy-n-propyl, 3-methoxy-n-propyl, methylamino-n-propyl, dimethylamino-n-propyl, di(n-butyl)amino-n-propyl, t-butoxycarbonylamino-n-propyl, 3-phenyl-n-propyl, 3-(2-pyridyl)-n-propyl, t-butoxycarbonyl, cyclopropyl, phenyl, 4-fluorophenyl, 4-methylphenyl, 3,4-dimethoxyphenyl, 2-aminophenyl, 4-biphenyl, 25 2-ethoxyphenyl, 4-((1-phenyl-pyrazol-2-yl)-aminosulfonyl)-phenyl, 4-cyclohexylphenyl, 4-(aminoethyl)phenyl, 4-(t-butoxycarbonylamino-ethyl)-



phenyl, -CH(CH<sub>3</sub>)-phenyl, benzyl, benzyloxy, 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl, 2-methoxybenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2-ethoxybenzyl, 3-ethoxybenzyl, 2-bromobenzyl, 3-bromobenzyl, 4-bromobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 3-iodobenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-trifluoromethoxybenzyl, 4-methoxycarbonylbenzyl, 2,3-dimethoxybenzyl, 2,4-dichlorobenzyl, 3,4-dichlorobenzyl, 2,4-difluorobenzyl, 2,5-difluorobenzyl, 3,4-difluorobenzyl, 3,4,5-trimethoxybenzyl, 2,4,6-trimethoxybenzyl, 4-carboxybenzyl, 3-nitrobenzyl, 4-nitrobenzyl, 2,4-dimethoxybenzyl, 3,4-dimethoxybenzyl, 3,5-dimethoxybenzyl, 3,4-difluorobenzyl, 3,5-di(trifluoromethyl)benzyl, 4-(dimethylamino)benzyl, 2-phenylethyl, 2-(4-bromophenyl)ethyl, 2-(3-methoxyphenyl)ethyl, 2-(4-methoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 2-(2-nitro-4,5-dimethoxyphenyl)ethyl, 3-(4-morpholinyl)-n-propyl, 2-(4-morpholinyl)ethyl, 2-(4-imidazolyl)ethyl, 1-adamantanyl, 1-adamantanyl-methyl, (2,5-dimethoxy-2,5-dihydro-fur-2-yl)methyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl-methyl, 3-pyridyl-methyl, 4-pyridyl-methyl, 2-(3,4-dimethyl-pyridyl), 2-(5-bromopyridyl), 2-(4,6-dimethyl-pyridyl), 2-(5-methyl-pyridyl), 3-(6-methoxy-pyridyl), 6-methylthio-2-pyridyl-carbonyl, thienyl-methyl, 2-thienylethyl, 4-pyridinyl, 1-naphthyl, 1-naphthyl-methyl, 1-(3,4-methylenedioxyphenyl)methyl, 2-(3,4-methylenedioxyphenyl)ethyl, 1-phenyl-2-(t-butoxycarbonyl)ethyl, -C(O)-C(OCH<sub>3</sub>)(CF<sub>3</sub>)-phenyl, -C(O)O-(2-isopropyl-5-methyl-cyclohexyl), 1-(4-ethoxycarbonyl-piperidinyl), 2-(3H-imidazol-4-yl)ethyl, 2-(1,2,3,4-tetrahydro-



alternatively when  $R^1$  and  $R^2$  are both bound to the same nitrogen atom,  $R^1$  and  $R^2$  are taken together with the nitrogen atom to which they are bound to form a group selected from 1-morpholinyl, 1-(4-(3-trifluoromethyl-phenyl)-piperazinyl), 1-(4-piperidinyl-piperidinyl), 1-(4-pyrrolidinyl-piperidinyl), 1-(4-phenyl-piperidinyl), 1-(3-hydroxy-piperidinyl), 1-(4-hydroxy-piperidinyl), 1-(3-hydroxymethyl-piperidinyl), 1-(3,5-dimethyl-piperidinyl), 1-(4-dimethylamino-piperidinyl), 1-(4-(3,4-methylenedioxyphenylmethyl)-piperazinyl), 1-(3-(diethylaminocarbonyl)-piperidinyl), 1-(4-t-butoxycarbonylamino-piperidinyl), 1-(2,3-dihydro-1H-pyrrolyl), 1-(4-[(4-chlorophenyl)-phenyl-methyl]-piperazinyl), 2-(1,2,3,4-tetrahydro-isoquinolinyl), 1-(4-t-butoxycarbonyl-piperazinyl), 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinolinyl), 4-(2,6-dimethyl-morpholinyl), 1-(4-benzyl-piperazinyl), 1-pyrrolidinyl, 1-(2,3-dihydro-pyrrolidinyl), 1-(3-hydroxy-pyrrolidinyl), 1-(3-(S)-hydroxy-pyrrolidinyl), 1-piperidinyl, 1-(3-ethoxycarbonyl-piperidinyl), 1-(4-ethoxycarbonyl-piperidinyl), 1-imidazolyl, 1-(2-(phenylamino-methyl)-N-pyrrolidinyl), 1-(3-(R)-dimethylamino-pyrrolidinyl), 1-(3-(R)-hydroxy-pyrrolidinyl), 1-(3,4-dihydroxy-2,5-bis-hydroxymethyl-pyrrolidinyl), 1-(3-(R)-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(S)-ethylamino-pyrrolidinyl), 1-(3-(R)-amino-pyrrolidinyl), 1-(3-(S)-amino-pyrrolidinyl), 1-(3-(R)-methylamino-pyrrolidinyl), 1-(3-(S)-methylamino-pyrrolidinyl), 1-(3-(N-methyl-N-t-butoxycarbonyl-amino)-pyrrolidinyl) or 1-(2-(3,5-dichlorophenyl)-3-methyl-5-carboxy-1,2,4-triazolyl);

$R^3$  is selected from the group consisting of phenyl and 4-fluorophenyl;

$L^1$  is selected from the group consisting of  $-CH_2-$ ,  $-CH(CH_3)-$  and  $-CH_2CH_2-$ ;



is selected from the group consisting of cyclooctyl, 1-acenaphthenyl, R-1-acenaphthenyl, S-1-acenaphthenyl, cyclohexyl, phenyl, 1-naphthyl, 2-naphthyl, 1,2,3,4-tetrahydro-naphthyl, 2-thienyl, benzothienyl, 4,5,6,7-tetrahydro-benzothienyl, bicyclo[3.1.1]hepten-2-yl, bicyclo[3.1.1]heptyl and (3aS)-2,3,3a,4,5,6-hexahydro-1H-phenalen-1-yl;

$R^5$  is selected from the group consisting of chloro, methyl, n-propyl and trifluoromethyl;

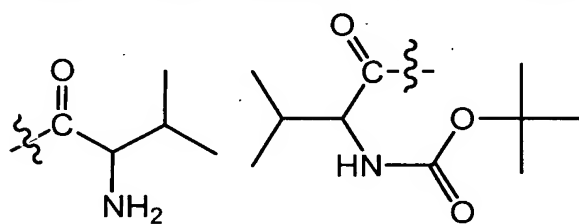
$R^7$  is selected from the group consisting of phenyl and 2-thienyl;  
or a pharmaceutically acceptable salt thereof.

5

5. A compound as in Claim 4 wherein

X is selected from the group consisting of  $-NR^1R^2$ ,  $-SR^1$  and  $-S-CH_2CH(CO_2H)-NH-C(O)-CH_3$ .

10  $R^1$  is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, t-butyl, dimethylaminoethyl, benzyl, phenylethyl,



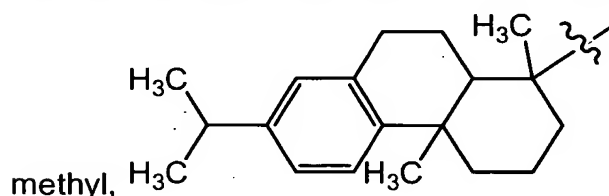
, 3-methyl-phenyl, 2-(3,4-dimethoxyphenyl)-ethyl, ethoxycarbonyl-methyl, dimethylamino-ethyl and 2-amino-2-methoxycarbonyl-ethyl;

15  $R^2$  is selected from the group consisting of hydrogen, methyl, methoxy, ethyl, ethoxycarbonyl-methyl, 2,2,2-trifluoroethyl, ethoxy, dimethylaminoethyl, n-butyl, t-butyl, n-propyl, di(n-butyl)amino-n-propyl, 3-phenyl-n-propyl, 3-(2-pyridyl)-n-propyl, cyclopropyl, phenyl, 4-fluorophenyl, 4-methylphenyl, 2-aminophenyl, 4-(t-butoxycarbonylamino-ethyl)-phenyl, 3,4-dimethoxyphenyl, 4-biphenyl, 2-ethoxyphenyl, 4-((1-phenyl-pyrazol-2-yl)-aminosulfonyl)-phenyl, 4-

20 (aminoethyl)-phenyl, benzyl, benzyloxy, 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl, 2-methoxybenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2-ethoxybenzyl, 3-ethoxybenzyl, 2-bromobenzyl, 3-bromobenzyl, 4-bromobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 3-iodobenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 4-

25 trifluoromethylbenzyl, 4-trifluoromethoxybenzyl, 4-methoxycarbonyl-benzyl, 2,3-dimethoxybenzyl, 2,4-dichlorobenzyl, 3,4-dichlorobenzyl, 2,4-difluorobenzyl, 2,5-difluorobenzyl, 3,4-difluorobenzyl, 3,4,5-trimethoxybenzyl, 2,4,6-trimethoxybenzyl, 4-carboxybenzyl, 3-nitrobenzyl, 4-nitrobenzyl, 2,4-dimethoxybenzyl, 3,4-dimethoxybenzyl, 3,5-dimethoxybenzyl, 3,4-

- difluorobenzyl, 3,5-di(trifluoromethyl)-benzyl, 2-phenylethyl, 2-(4-bromophenyl)ethyl, 2-(3-methoxyphenyl)ethyl, 2-(4-methoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 2-(2-nitro-4,5-dimethoxy-phenyl)ethyl, 3-(4-morpholinyl)-n-propyl, 2-(4-morpholinyl)ethyl, 2-(4-imidazolyl)ethyl,
- 5 adamantanyl, 1-adamantanyl-methyl, 2-(2,5-dimethoxy-2,5-dihydro-furyl)methyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl-methyl, 3-pyridyl-methyl, 4-pyridyl-methyl, 2-(3,4-dimethyl-pyridyl), 2-(5-bromopyridyl), 2-(4,6-dimethyl-pyridyl), 2-(5-methyl-pyridyl), 3-(6-methoxy-pyridyl), thienylmethyl, 2-thienylethyl, 1-naphthyl, 1-naphthyl-methyl, 1-(3,4-
- 10 methylenedioxyphenyl)methyl, 2-(3,4-methylenedioxyphenyl)ethyl, 2-furyl-



methyl, 2S-hydroxy-S-cyclopentyl-methyl, 2S-hydroxy-S-cyclohexyl-methyl, 2S-hydroxy-S-cycloheptyl-methyl, 2-phenoxy-ethyl and 2-(6-fluoro-2-indolyl)-ethyl;

- 15 alternatively when R<sup>1</sup> and R<sup>2</sup> are both bound to the same nitrogen atom, R<sup>1</sup> and R<sup>2</sup> are taken together with the nitrogen atom to which they are bound to form a group selected from 1-(4-(3-trifluoromethyl-phenyl)-piperazinyl), 1-(4-phenyl-piperidiny), 1-(4-piperidiny-piperidiny), 1-(4-(3,4-
- methylenedioxyphenyl-methyl)-piperazinyl, 1-(3-(diethylaminocarbonyl)-piperidiny), 1-(4-[(4-chlorophenyl)-phenylmethyl]-piperiaziny), 2-(1,2,3,4-
- 20 tetrahydro-isoquinoliny), 1-(4-t-butoxycarbonyl-piperazinyl), 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinoliny), 4-(2,6-dimethyl-morpholiny), 1-(4-benzyl-piperazinyl), 1-morpholiny, 1-pyrrolidiny, 1-(2,3-dihydro-pyrrolidiny), 1-piperidiny, 1-(3,5-dimethyl-piperidiny), 1-(3-hydroxymethyl-piperidiny), 1-(3-
- 25 ethoxycarbonyl-piperidiny), 1-(4-(ethoxycarbonyl)-piperidiny), 1-imidazolyl and 1-(2-(phenylamino-methyl)-N-pyrrolidiny);

L<sup>1</sup> is selected from the group consisting of -CH<sub>2</sub>- and -CH<sub>2</sub>-CH<sub>2</sub>-;



is selected from the group consisting of cyclooctyl, 1-acenaphthenyl, R-1-acenaphthenyl, S-1-acenaphthenyl, cyclohexyl, phenyl, 1-naphthyl and (3a-S)-2,3,3a,4,5,6-hexahydro-1H-phenalen-2-yl;

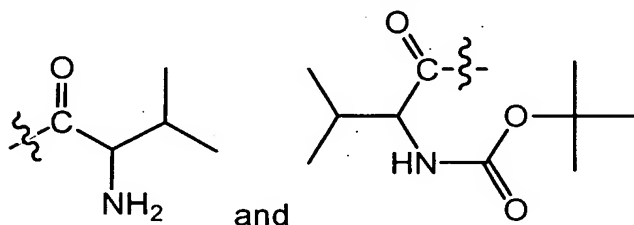
p is an integer from 0 to 2;

5  $R^7$  is 2-thienyl;

or a pharmaceutically acceptable salt thereof.

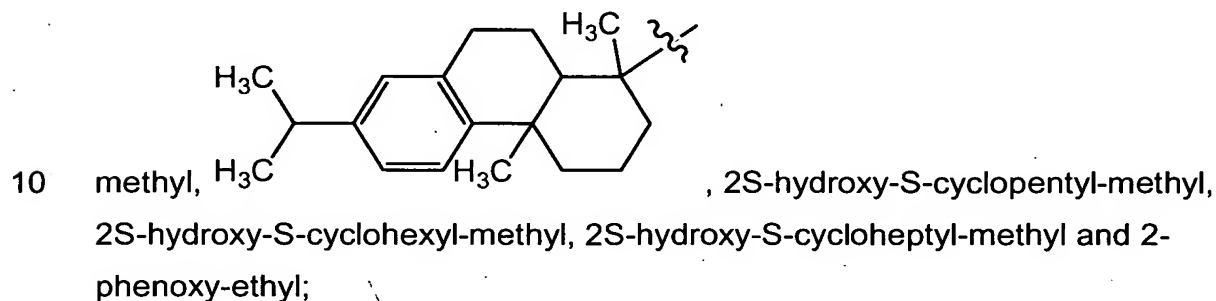
6. A compound as in Claim 5 wherein

10  $R^1$  is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, t-butyl, dimethylaminoethyl, benzyl, phenylethyl, 2-(3,4-dimethoxyphenyl)-ethyl, dimethylamino-ethyl, ethoxycarbonyl-methyl,



$R^2$  is selected from the group consisting of hydrogen, methyl, methoxy, ethyl, ethoxycarbonyl-methyl, ethoxy, dimethylaminoethyl, n-butyl, n-propyl, 15 di(n-butyl)amino-n-propyl, 3-phenyl-n-propyl, 3-(2-pyridyl)-n-propyl, cyclopropyl, phenyl, 4-fluorophenyl, 4-methylphenyl, 2-aminophenyl, 3,4-dimethoxyphenyl, 4-(t-butoxycarbonylamino-ethyl)-phenyl, 4-biphenyl, 2-ethoxyphenyl, 4-((1-phenyl-pyrazol-2-yl)-aminosulfonyl)-phenyl, 4-(aminoethyl)-phenyl, benzyl, benzyloxy, 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl, 2-methoxybenzyl, 20 3-methoxybenzyl, 4-methoxybenzyl, 2-ethoxybenzyl, 3-ethoxybenzyl, 2-bromobenzyl, 3-bromobenzyl, 4-bromobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 3-iodobenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 4-trifluoromethylbenzyl, 4-trifluoromethoxybenzyl, 4-methoxycarbonyl-benzyl, 2,3-dimethoxybenzyl, 2,4-dichlorobenzyl, 3,4-dichlorobenzyl, 2,4-difluorobenzyl, 2,5-difluorobenzyl, 3,4,5- 25 trimethoxybenzyl, 2,4,6-trimethoxybenzyl, 3-nitrobenzyl, 4-nitrobenzyl, 2,4-dimethoxybenzyl, 3,4-dimethoxybenzyl, 3,5-dimethoxybenzyl, 3,4-difluorobenzyl, 3,5-di(trifluoromethyl)-benzyl, 2-phenylethyl, 2-(4-

bromophenyl)ethyl, 2-(3-methoxyphenyl)ethyl, 2-(4-methoxyphenyl)ethyl, 2-(3,4-dimethoxyphenyl)ethyl, 2-(2-nitro-4,5-dimethoxy-phenyl)ethyl, 3-(4-morpholinyl)-n-propyl, 2-(4-morpholinyl)ethyl, 2-(4-imidazolyl)ethyl, 1-adamantanyl, 1-adamantanyl-methyl, 2-(2,5-dimethoxy-2,5-dihydro-furyl)methyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyridyl-methyl, 3-pyridyl-methyl, 4-pyridyl-methyl, 2-(3,4-dimethyl-pyridyl), 2-(5-bromopyridyl), 2-(4,6-dimethyl-pyridyl), 2-(5-methyl-pyridyl), 3-(6-methoxy-pyridyl), thienylmethyl, 2-thienylethyl, 1-naphthyl, 1-naphthyl-methyl, 1-(3,4-methylenedioxyphenyl)methyl, 2-(3,4-methylenedioxyphenyl)ethyl, 2-furyl-



alternatively when R<sup>1</sup> and R<sup>2</sup> are both bound to the same nitrogen atom,  
 15 R<sup>1</sup> and R<sup>2</sup> are taken together with the nitrogen atom to which they are bound to form a group selected from 1-(4-(3-trifluoromethyl-phenyl)-piperazinyl), 1-(4-phenyl-piperidiny), 1-(4-piperidiny-piperidiny), 1-(4-(3,4-methylenedioxyphenyl-methyl)-piperazinyl), 1-(3-(diethylaminocarbonyl)-piperidiny), 1-(4-[(4-chlorophenyl)-phenylmethyl]-piperiaziny), 2-(1,2,3,4-tetrahydro-isoquinoliny), 1-(4-t-butoxycarbonyl-piperazinyl), 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinoliny), 4-(2,6-dimethyl-morpholiny), 1-(4-benzyl-piperazinyl), 1-(3,5-dimethyl-piperidiny), 1-(3-hydroxymethyl-piperidiny), 1-(3-ethoxycarbonyl-piperidiny), 1-(4-(ethoxycarbonyl)-piperidiny), 1-piperidiny, 1-morpholiny, 1-pyrrolidiny, 1-imidazolyl, 1-(2,3-dihydro-pyrrolidiny), and 1-(2-(phenylamino-methyl)-N-pyrrolidiny);

p is an integer from 0 to 1;

R<sup>5</sup> is selected from the group consisting of methyl, n-propyl and trifluoromethyl;

or a pharmaceutically acceptable salt thereof.

7. A compound as in Claim 4 wherein

$R^0$  is  $-\text{CH}_2\text{-CH(OH)-CH}_2\text{-X}$ ;

X is  $-\text{NR}^1\text{R}^2$ ;

$R^1$  is selected from the group consisting of hydrogen, 2-(3,4-

5 dimethoxyphenyl)-ethyl, 1-(3,4-dimethoxyphenyl)-n-ethyl and amino-n-propyl;

$R^2$  is selected from the group consisting of hydrogen, methyl, n-butyl, 3-hydroxy-n-propyl, 3-methoxy-n-propyl, methylamino-n-propyl, dimethylamino-n-propyl, t-butoxycarbonylamino-n-propyl, N-methyl-N-t-butoxycarbonyl-amino-n-ethyl, 3-nitrobenzyl, 4-methoxycarbonyl-benzyl,  $-\text{CH}(\text{CH}_3)\text{-phenyl}$ , 4-pyridinyl, 10 1-(4-ethoxycarbonyl-piperidinyl) and 2-(3H-imidazol-4-yl)-ethyl;

alternatively when  $R^1$  and  $R^2$  are both bound to the same nitrogen atom,  $R^1$  and  $R^2$  are taken together with the nitrogen atom to which they are bound to form a group selected from 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinolinyl), 1-(4-[(4-chlorophenyl)-phenyl-methyl]-piperazinyl), 1-pyrrolidinyl, 1-(3-hydroxy-pyrrolidinyl), 1-(3-(S)-hydroxy-pyrrolidinyl), 1-(3-(R)-hydroxy-pyrrolidinyl), 1-(4-hydroxy-piperidinyl), 1-(3-(R)-dimethylamino-pyrrolidinyl), 1-(4-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(R)-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(R)-amino-pyrrolidinyl), 1-(3-(S)-amino-pyrrolidinyl), 1-(3-(R)-methylamino-pyrrolidinyl), 1-(3-(S)-methylamino-pyrrolidinyl), 1-(3-(S)-ethylamino-pyrrolidinyl), 1-(4-dimethylamino-pyrrolidinyl), 1-(3-(N-methyl-N-t-butoxycarbonyl-amino-pyrrolidinyl) or 1-(2-(3,5-dichlorophenyl)-3-methyl-5-carboxy-1,2,4-triazolyl);

$R^3$  is selected from the group consisting of phenyl and 4-fluorophenyl;

$L^1$  is selected from the group consisting of  $-\text{CH}_2-$  and  $-\text{CH}_2\text{CH}_2-$ ;



25 is selected from the group consisting cyclooctyl, 1-naphthyl, 1-acenaphthenyl, R-1-acenaphthenyl, S-1-acenaphthenyl, bicyclo[3.1.1]hepten-2-yl, bicyclo[3.1.1]heptyl and (3aS)-2,3,3a,4,5,6-hexahydro-1H-phenalen-1-yl.

p is an integer from 0 to 1;

$R^5$  is methyl;

30 q is 0;

or a pharmaceutically acceptable salt thereof.

8. A compound as in Claim 7 wherein

$R^1$  is selected from the group consisting of hydrogen, 1-(3,4-dimethoxyphenyl)-n-ethyl and amino-n-propyl;

5  $R^2$  is selected from the group consisting of hydrogen, methyl, n-butyl, 3-hydroxy-n-propyl, 3-methoxy-n-propyl, methylamino-n-propyl, dimethylamino-n-propyl, N-methyl-N-t-butoxycarbonyl-amino-n-ethyl, 3-nitrobenzyl, 4-methoxycarbonyl-benzyl, -CH(CH<sub>3</sub>)-phenyl, 4-pyridinyl and 2-(3H-imidazol-4-yl)-ethyl;

10 alternatively when  $R^1$  and  $R^2$  are both bound to the same nitrogen atom,  $R^1$  and  $R^2$  are taken together with the nitrogen atom to which they are bound to form a group selected from 2-(1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinoliny), 1-(4-[(4-chlorophenyl)-phenyl-methyl]-piperazinyl), 1-pyrrolidinyl, 1-(3-hydroxy-pyrrolidinyl), 1-(3-(R)-hydroxy-pyrrolidinyl), 1-(4-hydroxy-piperidinyl), 1-(3-(R)-dimethylamino-pyrrolidinyl), 1-(4-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(R)-t-butoxycarbonylamino-pyrrolidinyl), 1-(3-(R)-amino-pyrrolidinyl), 1-(3-(S)-amino-pyrrolidinyl), 1-(3-(R)-methylamino-pyrrolidinyl), 1-(3-(S)-methyamino-pyrrolidinyl), 1-(3-(S)-ethylamino-pyrrolidinyl), 1-(4-dimethylamino-pyrrolidinyl), 1-(3-(N-methyl-N-t-butoxycarbonyl-amino-pyrrolidinyl) or 1-(2-(3,5-dichlorophenyl)-3-methyl-5-carboxy-1,2,4-triazolyl);

20



is selected from the group consisting cyclooctyl, 1-naphthyl, 1-acenaphthenyl, R-1-acenaphthenyl, S-1-acenaphthenyl, bicyclo[3.1.1]hepten-2-yl, bicyclo[3.1.1]heptyl and (3aS)-2,3,3a,4,5,6-hexahydro-1H-phenalen-1-yl. or a pharmaceutically acceptable salt thereof.

25

9. A compound as in Claim 1 selected from the group consisting of 8-(R) acenaphthen-1-yl-3-(3-amino-2-(S)-hydroxy-propyl)-1-(4-fluorophenyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

30 8-(R) acenaphthen-1-yl-3-(3-amino-2-(R)-hydroxy-propyl)-1-(4-fluorophenyl)-1,3,8-triaza-spiro[4.5]decan-4-one;



8-(R)-Acenaphthen-1-yl-3-(3-dimethylamino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

3-(3-Amino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

5 3-(3-Dimethylamino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

8-(R)-Acenaphthen-1-yl-1-(4-fluoro-phenyl)-3-[2-(R)-hydroxy-3-(3-hydroxymethyl-piperidin-1-yl)-propyl]-1,3,8-triaza-spiro[4.5]decan-4-one;

10 3-(3-Amino-2-(R)-hydroxy-propyl)-8-cyclooctyl-1-(4-fluoro-phenyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

3-(3-Amino-2-(R)-hydroxy-propyl)-1-(4-fluoro-phenyl)-8-1-(S)-(3aS)-(2,3,3a,4,5,6-hexahydro-1H-phenalen-1-yl)-1,3,8-triaza-spiro[4.5]decan-4-one;

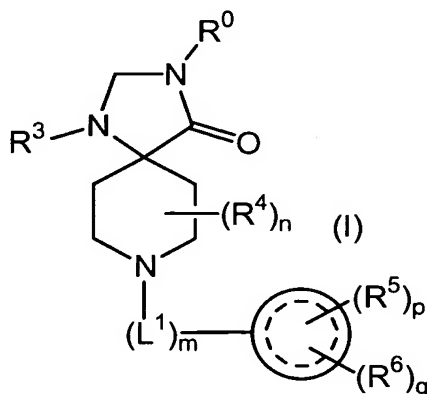
1-(4-Fluoro-phenyl)-3-[2-(R)-hydroxy-3-(3-hydroxy-propylamino)-propyl]-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

15 1-(4-Fluoro-phenyl)-3-[2-(R)-hydroxy-3-(3-methylamino-propylamino)-propyl]-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one;

3-[3-(3-Dimethylamino-propylamino)-2-(R)-hydroxy-propyl]-1-(4-fluoro-phenyl)-8-(8-methyl-naphthalen-1-ylmethyl)-1,3,8-triaza-spiro[4.5]decan-4-one and pharmaceutically acceptable salts thereof.

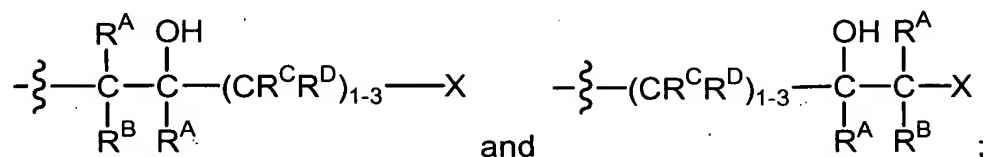
20

10. A compound of the formula (I)



wherein

$R^0$  is selected from the group consisting of



each  $R^A$  and  $R^B$  is independently selected from the group consisting of hydrogen and  $C_{1-4}$ alkyl;

- 5 each  $R^C$  and  $R^D$  is independently selected from the group consisting of hydrogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, nitro, cyano,  $N(R^E)_2$ , aryl,  $arC_{1-4}$ alkyl, heteroaryl or heterocycloalkyl; wherein the aryl,  $arC_{1-4}$ alkyl, heteroaryl or heterocycloalkyl substituent is optionally substituted with one or more substituents independently selected from hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, nitro, cyano or  $N(R^E)_2$ ;

each  $R^E$  is independently selected from the group consisting of hydrogen and  $C_{1-4}$ alkyl;

- 15 X is selected from the group consisting of  $-NR^1R^2$ ,  $-C(O)-NR^1R^2$ ,  $-NR^1-C(O)-R^2$ ,  $-OR^1$ ,  $-SR^1$ ,  $-SOR^1$ ,  $-SO_2R^1$ ,  $-S-(C_{2-4}alkyl)-NR^1R^2$ ,  $-S-(C_{2-4}alkyl)-C(O)O-C(CH_3)_3$ ,  $-SO-(C_{1-4}alkyl)-NR^1R^2$  and  $-SO_2-(C_{1-4}alkyl)-NR^1R^2$ ; wherein the alkyl portion of the  $-S-(C_{2-4}alkyl)-NR^1R^2$ ,  $-SO-(C_{1-4}alkyl)-NR^1R^2$  or  $-SO_2-(C_{1-4}alkyl)-NR^1R^2$  group is optionally substituted with one or more substituents independently selected from carboxy, hydroxy, hydroxy $C_{1-4}$ alkyl,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxycarbonyl or  $-CONR^1R^2$ ;

- 20 each  $R^1$  and  $R^2$  is independently selected from the group consisting of hydrogen,  $C_{1-8}$ alkyl,  $C_{1-8}$ alkoxy, cycloalkyl, cycloalkyl- $C_{1-4}$ alkyl, partially unsaturated carbocyclyl, aryl,  $arC_{1-4}$ alkyl,  $arC_{1-4}$ alkoxy, heteroaryl, heteroaryl- $C_{1-4}$ alkyl, heterocycloalkyl, heterocycloalkyl- $C_{1-4}$ alkyl,  $-C(O)-C_{1-6}alkyl$ ,  $-C(O)-aryl$ ,  $-C(O)-arC_{1-4}alkyl$ ,  $-C(O)-heteroaryl$  and  $-C(O)-heterocycloalkyl$ ; wherein the  $C_{1-8}$ alkyl, cycloalkyl, partially unsaturated carbocyclyl, aryl,  $arC_{1-8}alkyl$ , heteroaryl or heterocycloalkyl group, whether alone or part of a substituent group, is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano,  $-C(O)-C_{1-4}alkyl$ ,  $C_{1-4}$ alkoxycarbonyl,  $N(R^E)_2$ ,  $N(R^E)_2-C_{1-4}alkyl$ ,  $N(R^E)-C(O)C(CH_3)_3$ , aryl, aryloxy, cycloalkyl, heteroaryl, aryl substituted heteroarylaminosulfonyl or  $C_{1-6}alkylthio$ ;

- alternatively when  $R^1$  and  $R^2$  are both bound to the same nitrogen atom,  $R^1$  and  $R^2$  are taken together with the nitrogen atom to which they are bound to form a heteroaryl or heterocycloalkyl group; wherein the heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents
- 5 independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy,  $C_{1-4}$ alkoxycarbonyl, trifluoromethyl, trifluoromethoxy, nitro, cyano,  $N(R^E)_2$ , aryl, ar $C_{1-4}$ alkyl, heteroaryl, heterocycloalkyl, di( $C_{1-6}$ )alkylamino-carbonyl, t-butoxycarbonyl or arylamino- $C_{1-4}$ alkyl; wherein the aryl, ar $C_{1-4}$ alkyl, heteroaryl or heterocycloalkyl substituent is optionally further substituted with one or more
- 10 substituents independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano,  $N(R^E)_2$  or substituted phenyl; wherein the substituents on the phenyl are one or more independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or  $N(R^E)_2$ ;
- 15  $R^3$  is selected from the group consisting of aryl, ar $C_{1-6}$ alkyl and heteroaryl; wherein the aryl, ar $C_{1-6}$ alkyl or heteroaryl group is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or  $N(R^E)_2$ ;
- 20 n is an integer from 0 to 2;
- $R^4$  is selected from the group consisting of hydroxy,  $C_{1-4}$ alkyl and hydroxy substituted  $C_{1-4}$ alkyl;
- m is an integer from 0 to 1;
- $L^1$  is selected from the group consisting of  $C_{1-6}$ alkyl and  $C_{3-6}$ alkenyl;
- 25 wherein the double bond of the  $C_{3-6}$ alkenyl group is at least one carbon atom removed from the attachment point to the N atom; and wherein the  $C_{1-6}$ alkyl or  $C_{3-6}$ alkenyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro,  $C_{1-6}$ alkyl, fluorinated  $C_{1-6}$ alkyl or  $C_{1-6}$ alkoxy;



- 30 is selected from the group consisting of cycloalkyl, partially unsaturated carbocyclyl, aryl, heteroaryl and heterocycloalkyl;

p is an integer from 0 to 5;

$R^5$  is selected from the group consisting of hydroxy, carboxy, halogen,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, nitro, cyano,  $NR^1R^2$ , trifluoromethyl, trifluoromethoxy,  $C_{1-4}$ alkoxycarbonyl,  $-SO-NR^1R^2$ ,  $-SO_2-NR^1R^2$  and  $-C(O)-NR^1R^2$ ;

5 q is an integer from 0 to 1;

$R^6$  is selected from the group consisting of  $-(L^2)_{0-1}-R^7$ ;

$L^2$  is selected from the group consisting of  $-C_{1-6}$ alkyl-,  $-C_{2-4}$ alkenyl-,  $-C_{2-6}$ alkynyl-,  $-O-$ ,  $-S-$ ,  $-NH-$ ,  $-N(C_{1-4}alkyl)-$ ,  $-C_{1-6}alkyl-O-$ ,  $-C_{1-6}alkyl-S-$ ,  $-O-C_{1-6}alkyl-$ ,  $-S-C_{1-6}alkyl-$ ,  $-O-C_{2-6}alkyl-O-$ ,  $-S-C_{2-6}alkyl-S-$ ,  $-SO_2-$ ,  $-SO_2NH-$ ,  $-SO_2N(C_{1-4}alkyl)-$ ,  
 10  $-NH-SO_2-$ ,  $-N(C_{1-4}alkyl)-SO_2-$ ,  $-C(O)-O-$  and  $-O-C(O)-$ ;

$R^7$  is selected from the group consisting of aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl and heterocycloalkyl; wherein the aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents independently  
 15 selected from hydroxy, carboxy, halogen,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, nitro, cyano,  $N(R^E)_2$ , trifluoromethyl, trifluoromethoxy,  $C_{1-4}$ alkoxycarbonyl,  $-SO_2-N(R^E)_2$  and  $-C(O)-N(R^E)_2$ ;

or a pharmaceutically acceptable salt thereof.

20 11. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of Claim 1.

12. A pharmaceutical composition made by mixing a compound of Claim 1 and a pharmaceutically acceptable carrier.

25

13. A process for making a pharmaceutical composition comprising mixing a compound of Claim 1 and a pharmaceutically acceptable carrier.

14. A method of treating a disorder mediated by the ORL-1 receptor, in a  
 30 subject in need thereof comprising administering to the subject a therapeutically effective amount of the compound of Claim 1.

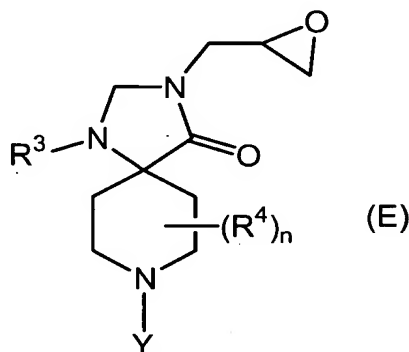
15. The method of Claim 14, wherein the disorder mediated by the ORL-1 receptor is selected from the group consisting of anxiety, depression, panic, mania, dementia, bipolar disorder, substance abuse, neuropathic pain, acute pain, chronic pain, migraine, asthma, cough, psychosis, schizophrenia, epilepsy, hypertension, obesity, eating disorders, cravings, diabetes, cardiac arrhythmia, irritable bowel syndrome, Crohn's disease, urinary incontinence, adrenal disorders, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, improved cognition, improved memory and mood stabilization.
16. A method of treating a disorder mediated by the ORL-1 receptor, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the composition of Claim 11.
17. A method of treating a condition selected from the group consisting of anxiety, depression, panic, mania, dementia, bipolar disorder, substance abuse, neuropathic pain, acute pain, chronic pain, migraine, asthma, cough, psychosis, schizophrenia, epilepsy, hypertension, obesity, eating disorders, cravings, diabetes, cardiac arrhythmia, irritable bowel syndrome, Crohn's disease, urinary incontinence, adrenal disorders, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, improved cognition, improved memory and mood stabilization, in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the compound of Claim 1.
18. A method of treating a condition selected from the group consisting of anxiety, depression, panic, mania, dementia, bipolar disorder, substance abuse, neuropathic pain, acute pain, chronic pain, migraine, asthma, cough, psychosis, schizophrenia, epilepsy, hypertension, obesity, eating disorders, cravings, diabetes, cardiac arrhythmia, irritable bowel syndrome, Crohn's disease, urinary incontinence, adrenal disorders, attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, improved cognition, improved memory and mood stabilization, in a subject in

need thereof comprising administering to the subject a therapeutically effective amount of the composition of Claim 7.

19. The use of a compound as in Claim 1 for the preparation of a medicament for the treatment of (a) anxiety, (b) depression, (c) panic, (d) mania, (e) dementia, (f) bipolar disorder, (g) substance abuse, (h) neuropathic pain, (i) acute pain, (j) chronic pain, (k) migraine, (l) asthma, (m) cough, (n) psychosis, (o) schizophrenia, (p) epilepsy, (q) hypertension, (r) obesity, (s) eating disorders, (t) cravings, (u) diabetes, (v) cardiac arrhythmia, (w) irritable bowel syndrome, (x) Crohn's disease, (y) urinary incontinence, (z) adrenal disorders, (aa) attention deficit disorder (ADD), (bb) attention deficit hyperactivity disorder (ADHD), (cc) Alzheimer's disease, for (dd) improved cognition, (ee) improved memory or (ff) mood stabilization, in a subject in need thereof.

15

20. A compound of the formula (E)



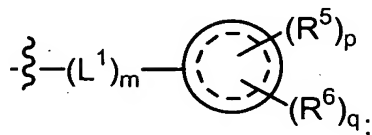
wherein

- 20  $R^3$  is selected from the group consisting of aryl, arC<sub>1-6</sub>alkyl and heteroaryl; wherein the aryl, arC<sub>1-6</sub>alkyl or heteroaryl group is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, trifluoromethyl, trifluoromethoxy, nitro, cyano or N(R<sup>E</sup>)<sub>2</sub>;

- each R<sup>E</sup> is independently selected from hydrogen or C<sub>1-4</sub>alkyl;
- 25 n is an integer from 0 to 2;

$R^4$  is selected from the group consisting of hydroxy, C<sub>1-4</sub>alkyl and hydroxy substituted C<sub>1-4</sub>alkyl;

Y is selected from the group consisting of hydrogen, C<sub>1-4</sub>alkyl, t-



butoxycarbonyl and

m is an integer from 0 to 1;

L<sup>1</sup> is selected from the group consisting of C<sub>1-6</sub>alkyl and C<sub>3-6</sub>alkenyl;

- 5 wherein the double bond of the C<sub>3-6</sub>alkenyl group is at least one carbon atom removed from the attachment point to the N atom; and wherein the C<sub>1-6</sub>alkyl or C<sub>3-6</sub>alkenyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C<sub>1-6</sub>alkyl, fluorinated C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkoxy;



- 10 is selected from the group consisting of cycloalkyl, partially unsaturated carbocyclyl, aryl, heteroaryl and heterocycloalkyl;

p is an integer from 0 to 5;

- R<sup>5</sup> is selected from the group consisting of hydroxy, carboxy, halogen, C<sub>1-6</sub>alkyl, hydroxy substituted C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, nitro, cyano, NR<sup>1</sup>R<sup>2</sup>,  
15 trifluoromethyl, trifluoromethoxy, C<sub>1-4</sub>alkoxycarbonyl, -SO-NR<sup>1</sup>R<sup>2</sup>, -SO<sub>2</sub>-NR<sup>1</sup>R<sup>2</sup> and -C(O)-NR<sup>1</sup>R<sup>2</sup>;

q is an integer from 0 to 1;

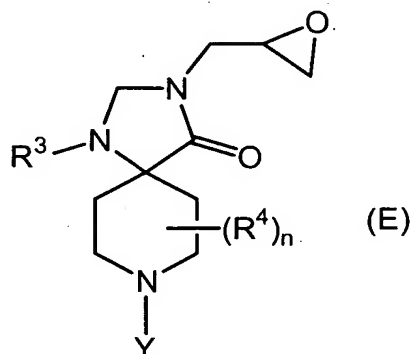
R<sup>6</sup> is selected from the group consisting of -(L<sup>2</sup>)<sub>0-1</sub>-R<sup>7</sup>;

- L<sup>2</sup> is selected from the group consisting of -C<sub>1-6</sub>alkyl-, -C<sub>2-4</sub>alkenyl-, -C<sub>2-6</sub>alkynyl-, -O-, -S-, -NH-, -N(C<sub>1-4</sub>alkyl)-, -C<sub>1-6</sub>alkyl-O-, -C<sub>1-6</sub>alkyl-S-, -O-C<sub>1-6</sub>alkyl-,  
20 -S-C<sub>1-6</sub>alkyl-, -O-C<sub>2-6</sub>alkyl-O-, -S-C<sub>2-6</sub>alkyl-S-, -SO<sub>2</sub>-, -SO<sub>2</sub>NH-, -SO<sub>2</sub>N(C<sub>1-4</sub>alkyl)-, -NH-SO<sub>2</sub>-, -N(C<sub>1-4</sub>alkyl)-SO<sub>2</sub>-, -C(O)-O- and -O-C(O)-;

- R<sup>7</sup> is selected from the group consisting of aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl and heterocycloalkyl; wherein the aryl,  
25 partially unsaturated carbocyclyl, cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, halogen, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, nitro, cyano, N(R<sup>E</sup>)<sub>2</sub>, trifluoromethyl, trifluoromethoxy, C<sub>1-4</sub>alkoxycarbonyl, -SO<sub>2</sub>-N(R<sup>E</sup>)<sub>2</sub> and -C(O)-N(R<sup>E</sup>)<sub>2</sub>;

or a pharmaceutically acceptable salt thereof.

21. A compound of the formula (E)



5 wherein

$R^3$  is selected from the group consisting of aryl, arC<sub>1-6</sub>alkyl and heteroaryl; wherein the aryl, arC<sub>1-6</sub>alkyl or heteroaryl group is optionally substituted with one or more substituents independently selected from halogen, hydroxy, carboxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, trifluoromethyl,

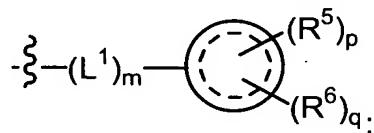
10 trifluoromethoxy, nitro, cyano or N(R<sup>E</sup>)<sub>2</sub>;

each R<sup>E</sup> is independently selected from hydrogen or C<sub>1-4</sub>alkyl;

n is an integer from 0 to 2;

$R^4$  is selected from the group consisting of hydroxy, C<sub>1-4</sub>alkyl and hydroxy substituted C<sub>1-4</sub>alkyl;

15 Y is selected from the group consisting of hydrogen, C<sub>1-4</sub>alkyl, t-



butoxycarbonyl and

m is an integer from 0 to 1;

$L^1$  is selected from the group consisting of C<sub>1-6</sub>alkyl and C<sub>3-6</sub>alkenyl; wherein the double bond of the C<sub>3-6</sub>alkenyl group is at least one carbon atom removed from the attachment point to the N atom; and wherein the C<sub>1-6</sub>alkyl or C<sub>3-6</sub>alkenyl group is optionally substituted with one to two substituents independently selected from hydroxy, fluoro, C<sub>1-6</sub>alkyl, fluorinated C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkoxy;

20





is selected from the group consisting of cycloalkyl, partially unsaturated carbocyclyl, aryl, heteroaryl and heterocycloalkyl;

p is an integer from 0 to 5;

- 5  $R^5$  is selected from the group consisting of hydroxy, carboxy, halogen,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, nitro, cyano,  $NR^1R^2$ , trifluoromethyl, trifluoromethoxy,  $C_{1-4}$ alkoxycarbonyl,  $-SO-NR^1R^2$ ,  $-SO_2-NR^1R^2$  and  $-C(O)-NR^1R^2$ ;

q is an integer from 0 to 1;

$R^6$  is selected from the group consisting of  $-(L^2)_{0-1}-R^7$ ;

- 10  $L^2$  is selected from the group consisting of  $-C_{1-6}$ alkyl-,  $-C_{2-4}$ alkenyl-,  $-C_{2-6}$ alkynyl-,  $-O-$ ,  $-S-$ ,  $-NH-$ ,  $-N(C_{1-4}alkyl)-$ ,  $-C_{1-6}alkyl-O-$ ,  $-C_{1-6}alkyl-S-$ ,  $-O-C_{1-6}alkyl-$ ,  $-S-C_{1-6}alkyl-$ ,  $-O-C_{2-6}alkyl-O-$ ,  $-S-C_{2-6}alkyl-S-$ ,  $-SO_2-$ ,  $-SO_2NH-$ ,  $-SO_2N(C_{1-4}alkyl)-$ ,  $-NH-SO_2-$ ,  $-N(C_{1-4}alkyl)-SO_2-$ ,  $-C(O)-O-$  and  $-O-C(O)-$ ;

- 15  $R^7$  is selected from the group consisting of aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl and heterocycloalkyl; wherein the aryl, partially unsaturated carbocyclyl, cycloalkyl, heteroaryl or heterocycloalkyl group is optionally substituted with one or more substituents independently selected from hydroxy, carboxy, halogen,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, nitro, cyano,  $N(R^E)_2$ , trifluoromethyl, trifluoromethoxy,  $C_{1-4}$ alkoxycarbonyl,  $-SO_2-N(R^E)_2$  and  $-C(O)-N(R^E)_2$ ;

- 20 or a pharmaceutically acceptable salt thereof.